In addition to solvent-free sample extraction, SPME is also a solvent-free sample introduction technique which facilitates design of a simple, low volume injection system. The net result is rapid desorption and good chromatographic separation, especially when flash-heated injectors are used. **Figure 7** illustrates 2.5 min extraction and separation of 28 Environmental Protection Agency volatile priority pollutants, which is over an order of magnitude faster than the standard purge and trap technique. This approach is particularly useful in combination with online SPME extraction. As eqn [6] indicates, it is possible to integrate sampling with a sample preparation step. This not only results in elimination of analyte losses to container walls and degradation during the transport, but also saves time and transport costs. This is particularly true when online SPME extraction is combined with field portable GCs.

Another interesting feature of SPME which is currently being explored includes speciation of analytes in complex matrices. The small amount of extracting phase does not disturb the equilibrium existing in the natural system and therefore allows quantitation of individual species or the determination of distribution constants in a multiphase system. In addition, the fibre can be made very specific, so separation using chromatographic systems may not be necessary. Therefore development of coupling between SPME with other analytical instrumentation, such as mass spectrometry and inductively coupled plasma–mass spectrometry will facilitate high sensitivity and a large throughput.

See also: **II/Extraction:** Solid-Phase Extraction; Solvent Based Separation. **III/Environmental Applications:** Solid-Phase Microextraction; **Solid-Phase Microextraction:** Overview.

Further Reading

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Solvent Based Separation

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R. G., P. M. Harper and Martin Hostrup,
CAPEC, Technical University of Denmark, Lyngby, Denmark

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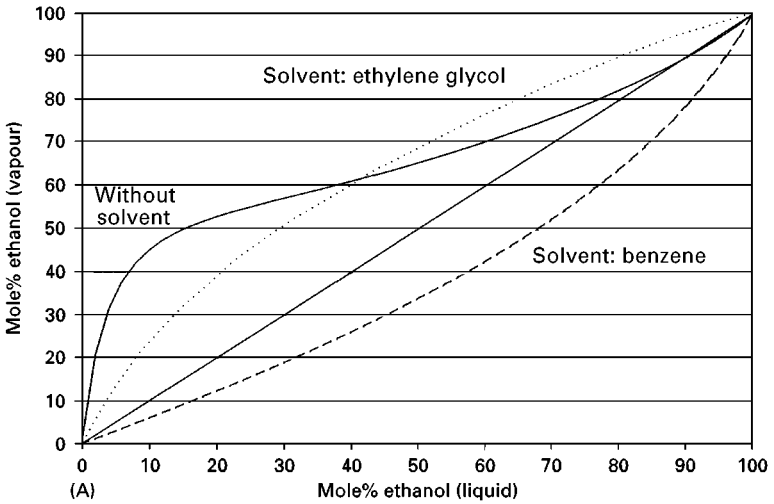
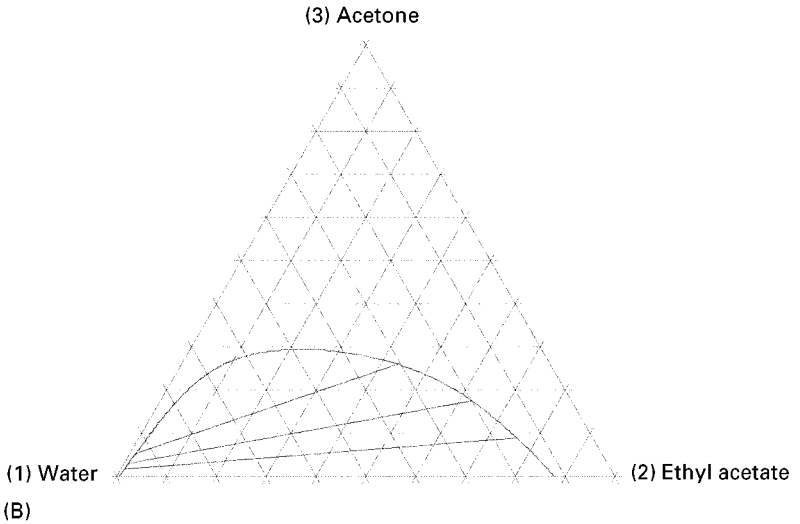
Introduction

Separation involves removal of one or more of the constituent parts from a mixture. A solvent is that constituent of a solution that is liquid in the pure state, is usually present in the larger amount, and has dissolved the other constituent (a solute) of the solution. The solute may be a solid, a liquid or a gas. The solvent may be a single compound or a mixture of compounds. Solvent-based separation techniques become necessary when separation or removal of a solute(s) from a mixture become difficult or infeasible by conventional separation techniques such as distillation. If the addition of a solvent causes a totally miscible liquid to split into two liquid phases and produce the necessary property difference, the solvent-based separation technique is commonly known as liquid–liquid extraction. If the addition of a solvent causes the coexisting vapour and liquid phases to have different properties, the solvent-based separation technique is called extractive distillation. **Figure 1**A and 1B highlight the change of the mixture properties as a result of the addition of a solvent. In Figure 1A, the difference between the properties of the liquid and vapour for the binary azeotropic mixture of ethanol–water with and without the addition of solvents is highlighted. It is clear from Figure 1A that addition of a solvent removes the barrier of the azeotropic condition. Figure 1B highlights through a ternary diagram that addition of the solvent causes the totally miscible binary liquid mixture (components 1 and 2) to split into two liquid phases, a solvent-rich phase and a solute-rich (1 or 2) phase.

Examples of industrial processes employing solvent-based separation techniques are numerous. Almost all chemical, petrochemical, biochemical and pharmaceutical processes employ one or more solvent-based separation techniques. In chemical and petrochemical processes, solvents are used mainly to separate components from liquid and/or gaseous mixtures, while in biochemical and pharmaceutical processes, solvents are typically employed for dissolving or removing solids. Use of a solvent to extract aromatic compounds from a petroleum by-product





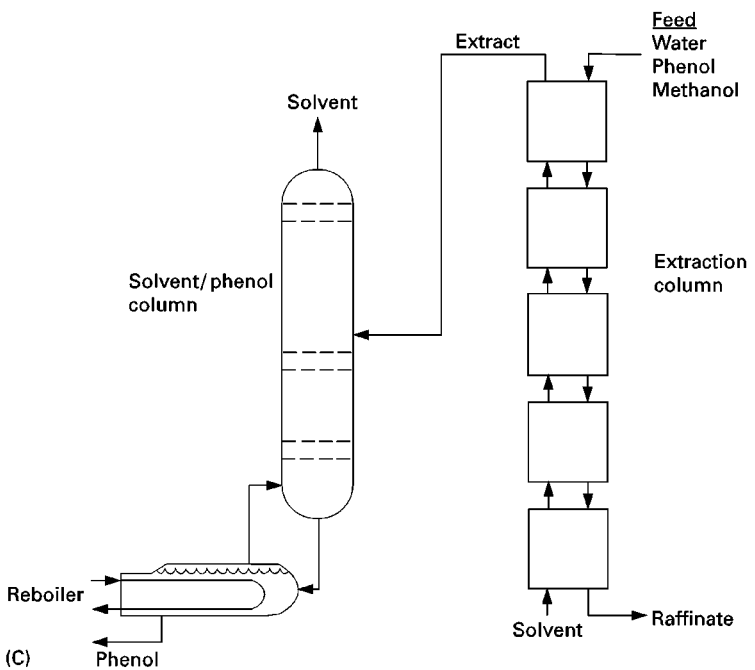


Figure 1 (A) VLE phase diagrams for ethanol–water (pressure 1 atm) with and without solvents (plotted on a solvent-free basis). (B) Ternary LLE diagram for acetone–water–ethyl acetate. (C) Process flowsheet for separation of phenol from wastewater.

Table 1 Classification of important solvent-based separation techniques

Separation technique	*Solute property*	*Number and identity of phase*	*Separation barrier*	*Separation phenomena*	*Solvent function*
Liquid–liquid extraction	Totally miscible solutes	Two liquid phases	Total miscibility	Property differences in liquid phases	Addition of solvent causes phase split
Extractive distillation	Solutes from azeotrope or are close boiling	Vapour and liquid phases	Azeotropes or relative volatilities	Property differences in vapour and liquid phases	Addition of solvent breaks the azeotrope but does not cause liquid phase split
Azeotropic distillation	Solutes from azeotrope or are close boiling	Vapour and two liquid phases	Azeotropes or relative volatilities	Property differences in vapour and two liquid phases	Addition of solvent breaks the azeotrope but also causes liquid phase split
Absorption	Absorbed gases in liquid	Vapour and liquid phases	Solubility of gases	Differences in solubility	Solvent must be able to dissolve the solute (gas)
Stripping	Entrained liquids in gases	Vapour and liquid phases	Solubility of liquids	Differences in solubility	Solvent must be able to dissolve the solute (liquid)
Leaching	Solid particles	Solid(s) and liquid phase	Solubility of solids	Differences in solubility	Solvent must be able to dissolve the solute (solid)

or removal of a chemical species (undesirable by-product or raw material) from a wastewater stream through solvent-based separation are typical examples of industrial application. Figure 1C illustrates the removal of phenol from water through solvent based liquid–liquid extraction. An important feature in this and most other vapour–liquid and/or liquid–liquid solvent-based separation techniques is that the solvent is recovered and recycled back to the solvent-based separation unit.

A logical criterion for classification of solvent-based separation techniques is the number and identities of the coexisting phases and the function of the solvent. **Table 1** gives a list of some of the well-known solvent-based separation techniques, classified in terms of the number and identities of the coexisting phases and function of the solvent. It can be noted from Table 1 that the selected solvent is directly related to the separation task and the separation technique and indirectly related to factors such as cost of operation, the efficiency of separation and the environmental impact. Therefore, solvent selection plays an important role in solvent-based separation. While solvents and solvent-based separation techniques have been known for a very long time, use of efficient search techniques, such as computer-aided molecular design (CAMD) and computer-aided database search, are fairly new. This article highlights the computer-aided methods and tools related to solvent selection.

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Solvent Selection: Problem Formulation

Problem formulation is an important first step in solvent selection as it is necessary first to define the functions of the solvent before attempting to find suitable candidates. Each problem, characterized in terms of solvent and solute properties, needs to address a set of issues related to separation task, performance, environmental impact and problem-specific (special) considerations. The solvent selection problem is formulated in terms of a set of properties (target properties) and their values (target values). A two-step procedure, consisting of a problem identification step (identifies the solvent functions and issues that need to be addressed) and a criteria for evaluation step (selects target properties and their target) is recommended.

Properties

The properties of the selected solvent define, to a large extent, the type of the solvent-based separation technique. Consider the binary azeotropic mixture of ethanol–water and the solvents benzene or ethylene glycol. If benzene is used as the solvent, the resulting solvent-based separation process is called azeotropic distillation because ethanol–water–benzene forms a heterogeneous azeotropic system, as shown in **Figure 2**A. If, on the other hand, ethylene glycol is used as a solvent, the solvent-based

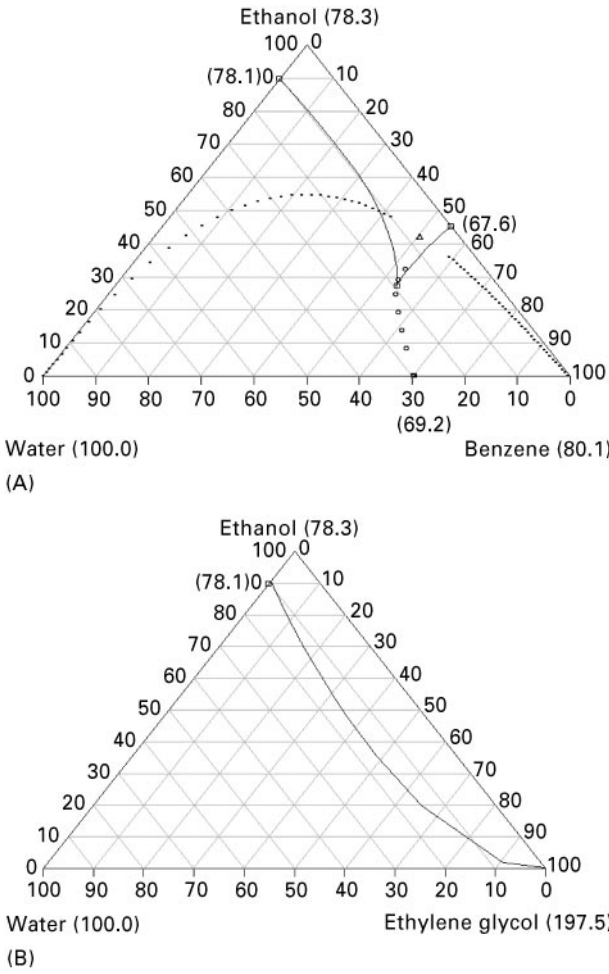

Figure 2 (A) Ternary VLLE diagram for ethanol–water–benzene (solvent). (B) Ternary homogeneous VLE diagram for ethanol–water–ethylene glycol (solvent). Key: …, heterogeneous liquid boiling surface; ○, vapour line; △, critical point; □, azeotropes. All temperatures in °C.

separation technique is called extractive distillation because ethanol–water–ethylene glycol forms a homogeneous azeotropic system, as shown in Figure 2B.

Table 2 gives a list of different types of solvent properties that may be considered in the selection/design of a solvent. These properties are classified in terms of pure component, mixture and environmental. **Table 3** expands on the nature of the environmental properties. While the pure component and environmental properties are usually available for a large number of chemical species, the mixture properties usually need to be estimated through suitable property prediction methods.

Problem Identification

Solvents are well known for their different applications and, therefore, functions. They may be employed as cleaning agents, as paint additives, as separating agents and many more. Each application of the solvent is related to different sets of desirable functions and undesirable effects (or functions). The main question that needs to be asked here is what functions will the selected solvent perform? The answer depends, to a large extent, on the properties of the solute and/or the mixture to be separated. Properties, for pure compounds and mixtures, provide a framework for classifying the different solvent functions and their undesirable effects in a systematic and structured way.

Criteria for Evaluation

Since in solvent selection problems, one is looking for alternatives that match approximately the desirable solvent functions but not the undesirable solvent effects, numerical values of properties can be used to evaluate candidate solvents. Based on the identified separation task, the question of which properties (target properties) should be considered in defining the solvent functions and what should be the property values (target values) is addressed in this step. The exact target values for the target properties are obtained by trial and error. However, if a known solvent is being substituted, then the target values are obtained from the solvent that needs to be substituted. In Table 2, two types of criteria for evaluation are shown – simple and general. As simple, the minimum number of properties that may define the desired solvent properties for each solvent based separation is highlighted, while as general, a comprehensive list of properties is highlighted.

Example

Consider the process from Figure 1C – the effluent water stream from an industrial process contains 7% w/w of phenol, which needs to be removed through liquid–liquid extraction. The desired solvent, when added to the phenol–water system, must cause a phase split such that the solvent-rich phase will contain significantly more phenol than water while the water-rich phase will contain very little phenol or solvent. It should be possible to separate easily the solvent from phenol. That is, the solvent must not form azeotrope, it must have a reasonable difference in boiling point and vapour pressure from phenol, and it must have a density lower than that of water in order to have free convection flow in the extraction column. If the solvent has a high environmental impact, the loss of the solvent through the water-rich phase will have to be reduced. If the solvent is unable to remove enough phenol, more solvent may need to be used. It should pose a low risk of explosion (the flash point temperature should be as high as possible).

Table 2 Solvent selection problem formulation with properties

Property	*Solvent design*									
	L–L Extraction		*Extractive distillation*		*Azeotropic distillation*		*Solid separation*		*Gas absorption*	
	Simple	*General*	*Simple*	*General*	*Simple*	*General*	*Simple*	*General*	*Simple*	*General*
Pure										
Solubility parameter	*		*		*		*			
Surface tension		*								*
Viscosity		*								
Boiling point	*	*	*	*	*	*				
Melting point	*	*	*	*	*	*	*	*	*	*
Density		*								
Vapour pressure			*	*	*	*			*	*
Heat of fusion								*		
Mixture										
Selectivity		*		*		*		*		*
Solvent loss.		*								
Solvent power		*		*		*		*		*
Distribution coefficient		*								
Phase split	*	*			*	*				
Azeotropes		*		*		*				
Mixture viscosity		*								
Henry's law constant									*	
Environmental	*	*	*	*	*	*	*	*	*	*

To ensure a minimal loss of the solvent to the water stream, the solvent should have very low miscibility in water and a high octanol–water partition coefficient. It should be possible to separate the solvent easily from phenol (must not form azeotrope, must have a reasonable difference in boiling point and vapour pressure from phenol, and must have a density lower than that of water in order to have free convection flow in the extraction column). For the process in Figure 1C, the target properties and their target values are given in **Table 4**.

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Table 3 Specific environmental concerns

Environmental property	*Health concern*	*Safety concern*	*Environmental concern*
Implicit			
Toxicity	*		*
Biological persistence			*
Chemical stability		*	
Reactivity	*	*	
Explicit			
Biodegradability			*
Vapour pressure	*	*	*
Henry's law constant in water			*
log *P*	*		*
Water solubility			*
Flash point		*	
Biological oxygen demand			*
Vapour density	*	*	
Evaporation rate	*	*	
LD_{50}	*		*
Ozone depletion potential			*

Solvent Selection: Methods and Tools

Methods

Solutions of solvent selection problems formulated above require a multistage approach (see **Figure 3**).

Table 4 Problem formulation for separation of phenol from wastewater

Target property	*Target value*
Partition coefficient (log *P*)	> 1.5
Solvent loss	< 0.0015
Liquid density at 298 K	< 0.95
Normal boiling point	< 450 K
Vapour pressure at 360 K	> 0.03 bar
Flash temperature	> 300 K
Selectivity	> 8
Capacity	> 2
Separation factor	> 80
Other properties	Must not form azeotrope with phenol
	Acceptable environmental properties

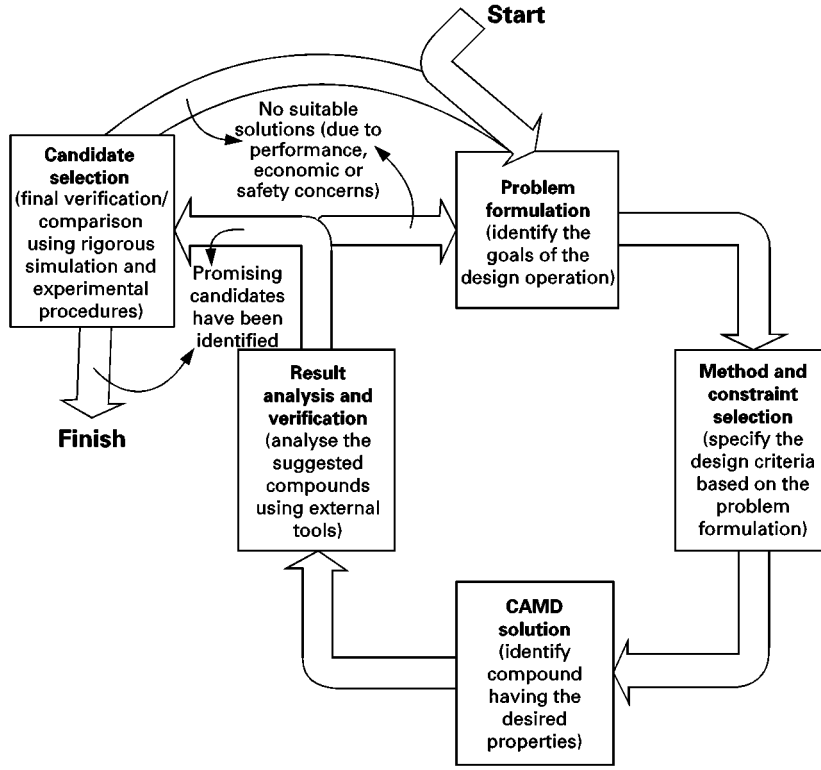
Start
No suitable solutions (due to performance, economic or safety concerns)
Candidate selection (final verification/ comparison using rigorous simulation and experimental procedures)
Problem formulation (identify the goals of the design operation)
Promising candidates have been identified
Result analysis and verification (analyse the suggested compounds using external tools)
Method and constraint selection (specify the design criteria based on the problem formulation)
Finish
CAMD solution (identify compound having the desired properties)

Figure 3 Multilevel approach to solvent selection.

After problem formulation, a list of feasible solvent alternatives is determined and ordered according to a specified criterion. The best feasible candidates are then analysed in terms of separation task, performance, environmental impact and special considerations in order to determine the most appropriate solvent(s). If none are found, it is necessary to go back to the problem formulation stage and relax some target property values or go back to the stage for determination of alternatives and use another search space. Thus, solvent selection is also a design problem requiring a trial-and-error solution approach.

List of solvent alternatives Determination of the list of solvent alternatives is based on the 'generate and test' paradigm. That is, first generate a list of solvent candidates and then analyse (test) the candidates to determine those that match the specified target property values. The methods available can be classified into three types: database search, CAMD and hybrid.

The database search approach involves a search in one or more databases for compounds that match the specified target property values. For this approach, an efficient search engine (or computer-aided technique) is needed. For solvent selection problems involving only pure component target properties, efficient search engines based on so-called pattern matching are available. Difficulties are encountered, however, when mixture properties are also included in the target properties and when the databases do not contain all the target properties for all the compounds. In such cases, an efficient and comprehensive search is almost impossible and reliable property estimation methods are needed.

In the CAMD technique, molecular structures of chemically feasible compounds are generated, the specified target properties for the generated molecules are estimated and those that match the specified target property values are included in the list of alternatives. The CAMD technique is therefore a more efficient search technique that is able to overcome the difficulties related to solvent selection problem formulations involving pure component as well as mixture target properties and incomplete databases. CAMD techniques, however, depend on the accuracy of the property estimation methods used for prediction of target properties for the generated molecules. The search space is not limited by the molecules present in a database but by the number of molecular structures that can be generated and by the application range of the property estimation methods used.

Combining the search based on databases with CAMD, a multilevel hybrid approach is obtained. In this approach, in level 1, a database search is carried out only with respect to the pure component target properties. This gives an idea of the types of molecules that are likely to be selected as solvents. Level 2

uses this information as initial estimate and employs CAMD to solve the solvent selection problem for the pure component and mixture properties that it can estimate with acceptable accuracy. At the end of level 2, a larger list of alternatives than level 1 is obtained. In level 3, those molecules that can be found in the database are identified and their target properties are verified, resulting in an updated list of alternatives. This list is now used for checking the remaining target properties (such as environmental properties and special properties that are found in special databases). Screening out the molecules that do not satisfy the target properties based on these databases produces a further refinement of the list of alternatives. Finally, in level 4, selected molecules from level 3 are investigated in terms of atomic structure, bond length, bond angle, energies, etc., through links to molecular modelling programs.

Final selection Since the list of alternatives contains more than one solvent, all of which match the specified target property values, it is necessary to determine the most appropriate solvent from this list. Therefore, it is necessary to define a selection criterion, for example, an objective function (F) that is either minimized or maximized. This objective function may be an explicit function of the target properties (see eqn [1]) or an implicit function of the target properties (see eqn [2]):

$$F = (S_P, S_S) \quad [1]$$

$$F = f(D_S(S_P, S_S), T(S_P, S_S), P(S_P, S_S)) \quad [2]$$

In the above equations, S_P is solvent power, S_S is selectivity, D_S is a vector of specified products, T is a vector of operating temperatures and P is a vector of operating pressures. Since the target properties of eqn [1] are known for the solvents in a generated and tested list of alternatives, use of eqn [1] simply means ordering the molecules in ascending order and selecting the optimal for further analysis (for example, pilot plant study). In this case, the solvent with the maximum value of F is regarded as the optimal solvent. In eqn [2], the evaluation of F needs other calculations (such as process simulation) in order to determine the values of D_S, T and P corresponding to an optimal F. Two solution approaches are commonly applied – an enumeration approach and a simultaneous solution approach. In the enumeration approach, the optimal value for F in eqn [2] is determined for each solvent through process simulation/optimization, generating a set of values for F, D_S, T and P corresponding to each solvent in the generated list of alternatives. The optimal solvent then corresponds to the minimum (or maximum) F in the generated set. In the simultaneous solution approach, the solvent identity is an integer variable and adding it as an optimization variable in the process optimization problem gives a mixed integer nonlinear programming (MINLP) problem formulation, which determines the optimal solvent and the optimal F simultaneously.

Tools

From the above section, it is clear that the tools that are needed for solution of the solvent selection problem are databases, search engines, property estimation methods, process simulators and numerical methods (such as a MINLP-solver). It should be noted that all the tools might not be necessary for all solvent selection problems. Also, different sets of tools are needed depending on the chosen method of solution. In this article, only the use of search engines with the hybrid approach, which includes database search, CAMD and property prediction, is highlighted. **Table 5** gives a list of various tools that may be used in solving solvent selection problems.

Search engine The hybrid generate-and-test approach (search engine–CAMD algorithm) has four levels. Each level has its own generate-and-test algorithms. Higher levels use additional molecular structural information compared with lower levels. Levels 1–2 are group contribution based (thereby employing macroscopic representation of the molecule), while levels 3–4 are based on atomic (microscopic) representation of the molecule. Switch from level 1–2 to 3–4 needs a conversion of macroscopic representation to microscopic representation.

Level 1 This level generates sets of building blocks (*fragments*) by combining first-order functional groups. These sets are capable of forming at least one feasible molecular structure. Simultaneous calculation of related properties (that are dependent only on first-order groups) and screening of the generated structures is performed to control the problem size and execution time. The algorithm here is based on a modified set of rules. Building blocks are classified according to type. Feasibility rules are based on the number of groups from a specific class a compound may contain. Valency rules are used to determine the number of groups with one, two, three and four connections that are to be used in molecule structure generation. The main steps of the level 1 algorithm are illustrated in **Figure 4**.

Level 2 This level generates molecular structures by combining elements of the individual fragment sets

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Table 5 List of tools for solvent selection problems

Tool	*Type*	*Contact information*
ProCAMD	CAMD	CAPEC
Synapse	CAMD	Molecular Knowledge Systems, Inc.
EFDB	Electronic database (environmental fate)	Syracuse Research Corporation
ChemBank—RTECS	Electronic database (health, safety, physical properties, environmental data)	SilverPlatter Information Inc.
Dortmund Data Bank	Electronic database (mixture and physical properties)	DDBST GmbH
PHYSPROP	Electronic database (physical properties)	Syracuse Research Corporation
SOLVDB	Electronic database (solvents)	Syracuse Research Corporation
NIST WebBook	Online database (physical properties)	NIST
CS Chemfinder	Online database (physical properties, links to other sources)	Cambridge Soft Inc.
SMSWIN	Phase behaviour calculations	AstraZeneca
Process Design Studio	Phase behaviour calculations	CAPEC
ChemDraw 5.0 Ultra	Property prediction	Cambridge Soft Inc.
ACD/Labs Physico-Chemical Laboratory	Property prediction	Advanced Chemistry Development inc.
Cranium	Property prediction	Molecular Knowledge Systems, Inc.
ProPred 2.5	Property prediction	CAPEC

from level 1 to form molecular structures. First- and second-order groups are considered. The main feature of this algorithm is that it is pseudorecursive, all allowed combinations are considered, and efficiency is maintained by continuous removal of duplicate structures. Also, the combination rules satisfy conditions of chemical feasibility. Use of second-order groups allows the estimation method to differentiate between some isomers.

Level 3 In this level, the selected candidates from level 2 are given an atomic representation. Note that the atomic representation also defines the connectivity of the molecules. Therefore, property prediction methods based on connectivity indices can be employed to predict properties that could not be predicted earlier (due to unavailable group contributions) or to verify previously estimated values.

Level 4 In this level, generation and testing enters an interactive mode. For any selected candidate from level 3, it is possible to use molecular modelling programs such as MOPAC or Chem3D from Cambridge Soft Corp. A three-dimensional graph (or

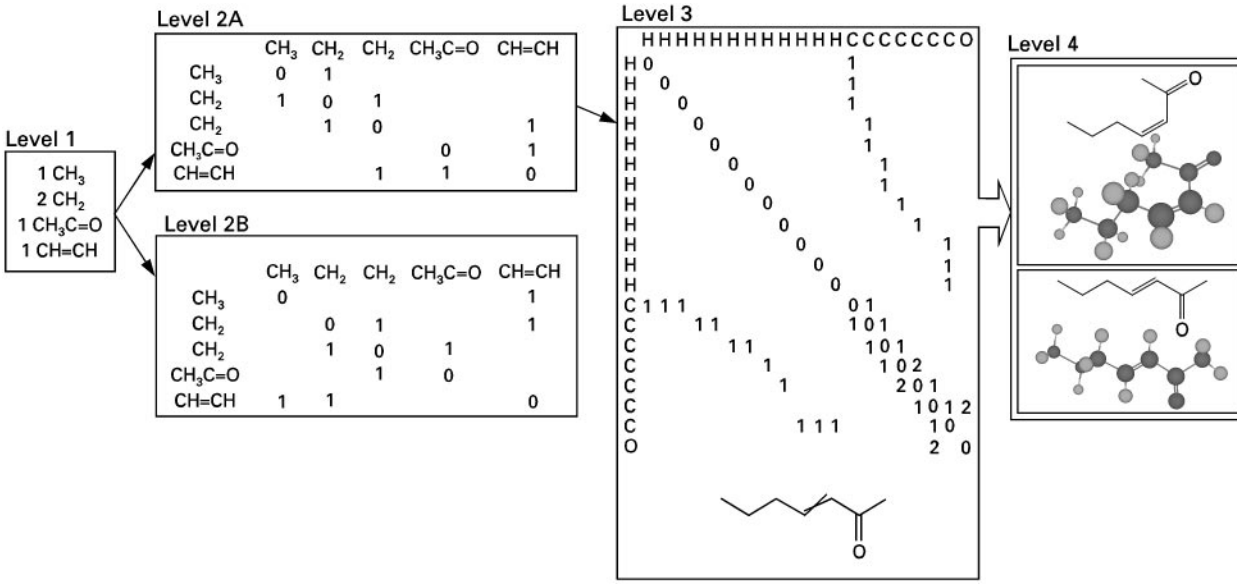

Figure 4 Hybrid CAMD search engine.

molecular model) is created by applying a set of standard or default bond lengths and angles for the various types of connections. As a result the true molecular model of a compound, which can be further analysed in terms of conformers, stability, properties, etc., is obtained.

Application Examples

Problems

Solutions of solvent selection problems with the database search approach and the hybrid approach are illustrated. Tools listed in Table 5 have been used for solution of these problems, which involve solvent-based vapour–liquid, liquid–liquid and solid–liquid separations. For the removal of morphine, all the solution steps for solvent selection with the hybrid approach are highlighted. For the other examples, only the problem formulation in terms of target properties and the final results are presented. Also, for solution with the database search approach, only pure component target properties have been considered.

Database Search Approach

For the seperation of phenol from water by liquid–liquid extraction, solution of the problem (as defined in Table 4) finds, among others, butyl acetate and toulene as solvents that match the pure component target properties.

For the purification of ethanol from a binary mixture of ethanol–water, solvents for extractive or azeotropic distillation are sought. The pure component target properties are: normal boiling point (T_b) < 473 K; melting point (T_m) > 270 K; flash point (F_T) > 320 K; solubility paramater (δ) between 15 and 20 $MPa^{1/2}$ for azeotropic distillation or 28 and 35 $MPa^{1/2}$ for extractive distillation. Note that δ of ethanol is around 26 $MPa^{1/2}$ and that of water is around 47.8 $MPa^{1/2}$. A value of δ far from water and closer to ethanol will be selective to ethanol and will likely cause a phase split. Benzene, toluene and cyclohexane satisfy the target property values for azeotropic distillation. Ethylene glycol satisfies the requirements for extractive distillation. Figure 2A and 2B also confirm this result.

For the separation (removal) of phenol present as a solid, a solvent is needed to dissolve it. The solvent target properties may be defined with T_m > 270 K, T_b < 473 K and 23.5 < δ < 25.5 $MPa^{1/2}$. A search of the database gives furfuryl alcohol, aniline, *N*,*N*-dimethylformamide and furfural. The solvent function of aniline related to dissolving solid phenol is validated through the computed solid–liquid phase diagram for the phenol–aniline mixture (see **Figure 5**).

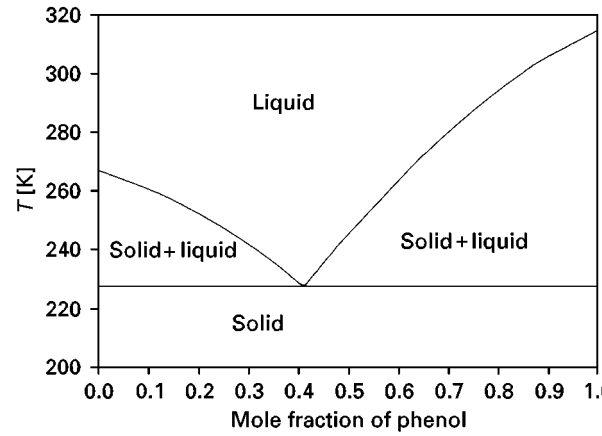

Figure 5 Computed SLE phase diagram for aniline–phenol.

Hybrid Approach

The solvent selection problem for the removal of phenol from wastewater has been solved with the ProCAMD (see Table 5). The summarized results from ProCAMD are shown in **Figure 6**. Compared with butyl acetate and toluene, this solvent has been found to have a higher *F* (eqn [1]) and is environmentally acceptable.

Identification of a solvent for morphine

Problem formulation In the production of morphine a solvent is needed for dissolving the solid. Known solvents for morphine include cyclohexane, tetrachloromethane, toluene and benzene. It is desired to find alternative solvents capable of dissolving morphine. Furthermore, in order not to contaminate the product with toxic substances, in case of solvent inclusions after crystallization, the compound should be nonaromatic and have a low toxicity.

Constraint selection Solubility is a mixture property. To be able to predict solubility to some degree of accuracy it is necessary to have access to a method for calculation of activity coefficients. For complex compounds (such as morphine) very few group-contribution-based property estimation methods are able to describe the molecular structure (see **Figure 7**). Therefore, the search for alternative solvents is carried out using pure component properties as criteria for evaluation. It is well known that two compounds having similar solubility parameters (δ) are highly likely to be miscible. The search for solvents for morphine can therefore be expressed as a search for compounds being liquid at ambient temperatures and having a solubility parameter as close as possible to that of morphine (δ = 26.3 $MPa^{1/2}$).

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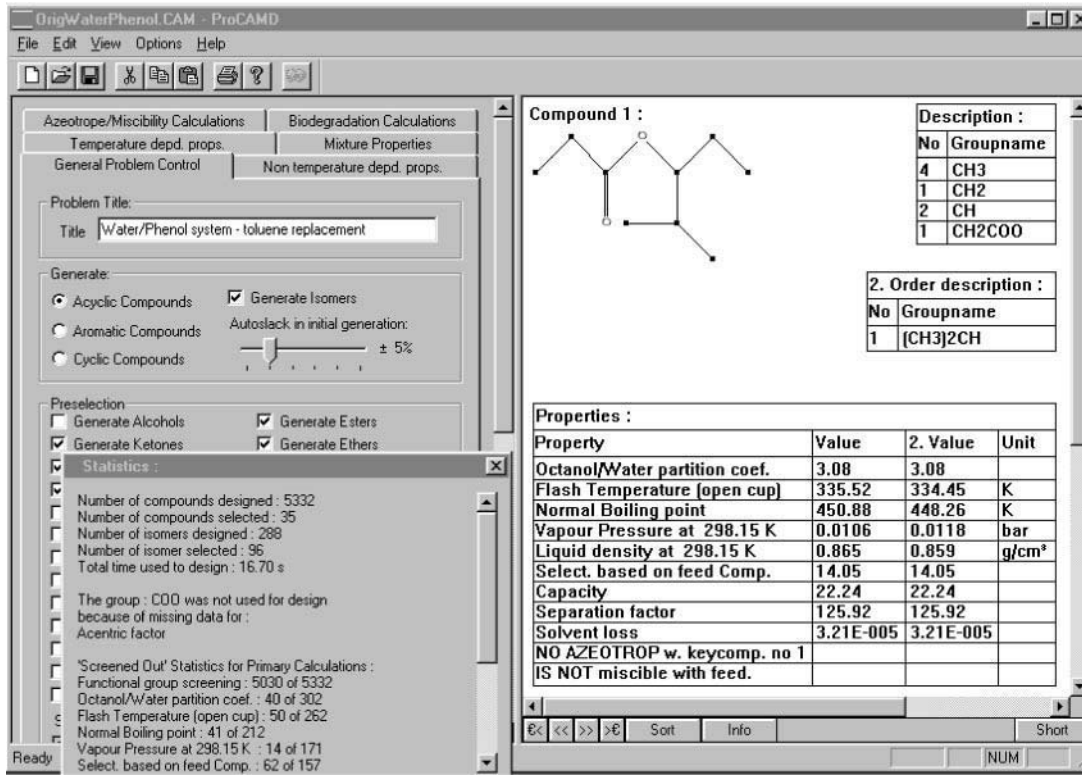
OrigWaterPhenol.CAM - ProCAMD
File Edit View Options Help
Azeotrope/Miscibility Calculations
Biodegradation Calculations
Temperature depd. props.
Mixture Properties
General Problem Control
Non temperature depd. props.
Problem Title:
Title Water/Phenol system - toluene replacement
Generate:
Acyclic Compounds
Aromatic Compounds
Cyclic Compounds
Generate Isomers
Autoslack in initial generation:
± 5%
Preselection
Generate Alcohols
Generate Esters
Generate Ketones
Generate Ethers
Statistics :
Number of compounds designed : 5332
Number of compounds selected : 35
Number of isomers designed : 288
Number of isomer selected : 96
Total time used to design : 16.70 s
The group : COO was not used for design because of missing data for :
Acentric factor
'Screened Out' Statistics for Primary Calculations :
Functional group screening : 5030 of 5332
Octanol/Water partition coef. : 40 of 302
Flash Temperature (open cup) : 50 of 262
Normal Boiling point : 41 of 212
Vapour Pressure at 298.15 K : 14 of 171
Select. based on feed Comp. : 62 of 157
Ready
Compound 1 :
Description :
No Groupname
4 CH3
1 CH2
2 CH
1 CH2COO
2. Order description :
No Groupname
1 (CH3)2CH
Properties :
Property Value 2. Value Unit
Octanol/Water partition coef. 3.08 3.08
Flash Temperature (open cup) 335.52 334.45 K
Normal Boiling point 450.88 448.26 K
Vapour Pressure at 298.15 K 0.0106 0.0118 bar
Liquid density at 298.15 K 0.865 0.859 g/cm³
Select. based on feed Comp. 14.05 14.05
Capacity 22.24 22.24
Separation factor 125.92 125.92
Solvent loss 3.21E-005 3.21E-005
NO AZEOTROP w. keycomp. no 1
IS NOT miscible with feed.
Sort
Info
Short
NUM

Figure 6 Results for phenol–wastewater separation (screenshot from ProCAMD).

Design specifications

- *Compound type* acyclic alkanes, ethers, esters, aldehydes, ketones, alchohols;
- $T_b > 350$ K; $T_m < 273$ K;
- $22 < \delta < 30$ (exclusion of the lowest ranking candidates);
- *performance measure* $|26.3 - \delta|$ should be as low as possible.

Generation of alternatives The ProCAMD package (see Table 5) was used, generating 348 candidates fulfilling the requirements. After performing a structure search to identify substances with known CAS registry numbers two candidates, 1,5-pentanediol and acetol, were selected based on having a solubility parameter close to that of morphine.

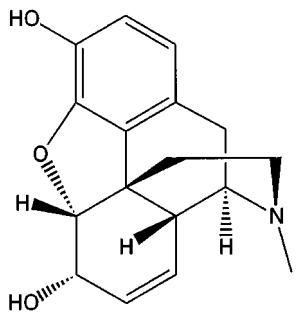

Figure 7 Molecular structure of morphine.

Analysis and verification To verify the predicted values of the properties used as design specifications a search in available databases was carried out and the experimental values compared to the predicted. Furthermore the RTECS database (see Table 5) was consulted in order to investigate the health and environment properties of the selected compounds. The result of the investigations and the predicted properties are shown in **Table 6**.

Candidate selection From the data listed in Table 6 it is clear to see that among the known and generated solvents 1,5-pentanediol is the most promising candidate and should be selected for further testing in an experimental setting.

Future Developments

As current and future separation problems become more difficult due to complex molecular structure of solutes, changes in environmental regulations and demands for material and energy conservation, the solvent selection problem is also becoming more difficult. It is no longer feasible to attempt to solve the solvent selection problem with a single database. Computer-aided techniques provide the necessary framework to solve the current and future solvent selection problems. The current hybrid approaches,

Table 6 List of solvents for separation of morphine

Solvent	*CAS-NO*	*Predicted*			*Experimental*			*Compound class (RTECS)*
		T_b (K)	T_m (K)	δ (MPa$^{1/2}$)	T_b (K)	T_m (K)	δ (MPa$^{1/2}$)	
Benzene	71-43-2				353.24	278.68	18.73	C,D,M,T,S
Toluene	108-88-3				383.78	178.18	18.32	C,M,T,S
CCl_4	56-23-5				349.79	250.33	17.55	C,D,M,T,S
Cyclohexane	110-82-7				353.87	279.69	16.76	M,S
1,5-Pentanediol	111-29-5	491	253	27.0	512.15	257.15	26.45	S
Acetol	116-09-6	418	226	27.2	418.65	256.15	25.75	M

D, drug; S, primary irritant; T, reproductive-effector; M, mutagen; C, tumorigen.

however, need to integrate aspects of molecular modelling and computational chemistry before acceptable solutions to problems involving complex solutes and tight environmental regulations can be obtained. Finally, it should be noted that having a good solvent means easier design/operation of the solvent-based separation technique. Therefore, it is important to formulate correctly the solvent selection problem and to find reliable results in the form of optimal solvents.

Further Reading

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DropBooks

Steam Distillation

L. Ramos, Free University, Amsterdam, The Netherlands

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Sample preparation is nowadays the limiting step in the trace analysis of organic pollutants in environmental and biological samples. Looking forward to the laboratory of the future, versatile and universal sample enrichment techniques are required, which can produce fast and valid data, with low costs in terms of solvent consumption and operator involvement. A selectivity higher than that of the classical exhaustive extraction methods or the simultaneous elimination of the interference material could be an additional requirement, as it would reduce the amount of solvents and adsorbents used by reducing or eliminating the subsequent clean-up step. Possible additional benefits deriving from a low manual manipulation of the samples would be a reduction in the risk of contamination and loss of the analytes, as well as an easier automation of the process.

Steam distillation extraction–solvent extraction (SDE) has been presented as such a universal sample enrichment technique. SDE allows the simultaneous extraction, clean-up and concentration of the target compounds in a closed system, with short analysis times (1–8 h) and by using small amounts of organic solvents (a few mL). This paper reviews this assumption for the case of the analysis of less volatile organic pollutants in environmental samples. The SDE advantages and shortcomings for such an analysis have been discussed.

Introduction

The monitoring of toxic organic chemicals in environmental and biological samples is a major concern in many different fields. However, the large variety of compounds of interest, the differences existing in